Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

The hidden allergen: Triton X-100, a derivative of polyethylene glycol

To the Editor:

We applaud the authors on their publication summarizing an approach to allergic reactions and mRNA coronavirus disease (COVID) vaccines (Pfizer-BioNtech, Moderna) given the rapidly evolving evidence during the current global pandemic.[1] Although the specific mechanism of allergy and the inciting antigen of reactions to mRNA COVID vaccines have not been confirmed, polyethylene glycol (PEG) is hypothesized to be the culprit.

Although the current understanding is that PEG itself has not previously been used in a vaccine, this view may be erroneous. Triton X-100 (TX-100) is a nonionic detergent that has a PEG-based tail group (Figure 1).[2] Other names for TX-100 include octoxinol and polyethylene glycol mono(*p*-(1,1,3,3-tetramethylbutyl) phenyl) ether. TX-100 is commonly used in laboratories and is applied to vaccines at different stages of the manufacturing process. It is listed as an excipient in certain vaccines including split virus influenza vaccines. It is noteworthy that vaccines containing TX-100 are not listed in easily recognizable language as containing PEG in product monographs reviewed.[3,4]

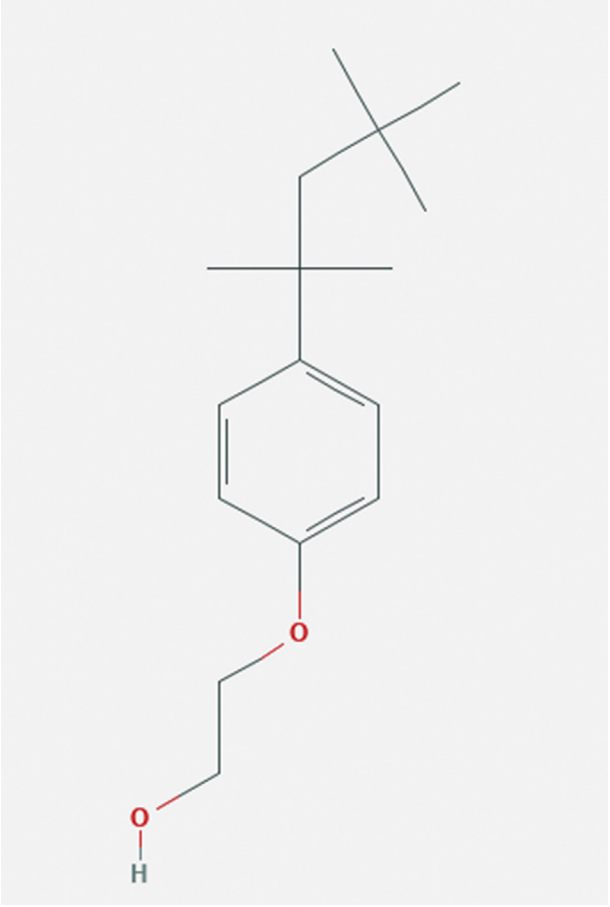

FIGURE 1. Chemical structure of TX-100.

Although TX-100 amounts in vaccines may be insufficient to induce allergic reactions in most patients, possible hypersensitivity to this component may be a concern in those who have an allergy to PEG. The Pfizer-BioNTech and Moderna COVID vaccines contain 0.05 mg of the ALC-0159 (ie, 2-[polyethylene glycol-2000]-*N*,*N*-ditetradecylacetamide) per 0.3 mL dose and an estimate of 0.1 mg of PEG 2000 dimyristoyl glycerol (DMG-PEG 2000) per 0.5 mL dose, respectively.[5,6] Although it appears that the polyethylene oxide chain content of seasonal influenza vaccines containing TX-100 is comparable to that of mRNA COVID-19 vaccines in one study, [7] the polyethylene oxide chains in the COVID vaccines consist of more ethylene oxide units per molecule compared with TX-100 (44-46 units as opposed to 9-10 units). Because the risk of sensitization generally appears to be greater with higher-molecular-weight PEGs containing longer polyethylene oxide chains, those who have experienced a reaction to vaccines containing TX-100 may be at increased risk of reaction to currently authorized mRNA PEG-containing COVID vaccines, as well as vaccines containing cross-reactive polysorbates.

Although the authors are aware of a case of 2 episodes of probable anaphylaxis following initial and repeat administration of an annual influenza vaccine containing TX-100, to date, there are no published reports of anaphylaxis to TX-100. Given the increasing number of reports of allergic reactions to PEG, and the concealed relationship between TX-100 and PEG, scrutiny of labeling of vaccines containing TX-100 is crucial. TX-100 may be an unrecognized contributor to allergic reactions to vaccines, especially in cases of uncertainty, and further exploration of this potential allergen may be warranted.

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